Acute Painful Nodules in a Young Healthy Adult

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Case Report

A previously healthy 19-year-old man with no significant past medical history presented to the emergency room with six days of worsening fever, headache, and sore throat and a one-day history of tender nodules on the extremities, abdomen, and neck. The patient reported no recent medications, vaccination, illicit substances, or travel prior to this event. He reported no skin problems in the past or family history of skin conditions. Physical examination revealed multiple, tender, 2 to 3cm erythematous nodules distributed haphazardly on the lower extremities, trunk, hands, and neck (Figures 1A–1B). The mucous membranes, genitals, and palms and soles were spared. Punch biopsy from the most prominent and painful nodule on the patient's left thigh was obtained for histopathological analysis (Figure 1C). Initial laboratory results were significant for elevated erythrocyte sedimentation rate of 92mm/hr (normal: 0–20mm/hr), C-reactive protein of 138.6mg/L (normal: 0–10mg/L), antistreptolysin O of 200units/mL (normal: 0–100 units/mL), and white blood cell count of 8,100/mm^3 (normal: 4,000–12,000/mm^3) with 75.1% neutrophils (normal: 54–62%). Blood, wound, throat, and cerebrospinal fluid cultures were sent for evaluation.

Diagnosis

Subcutaneous Sweet's syndrome

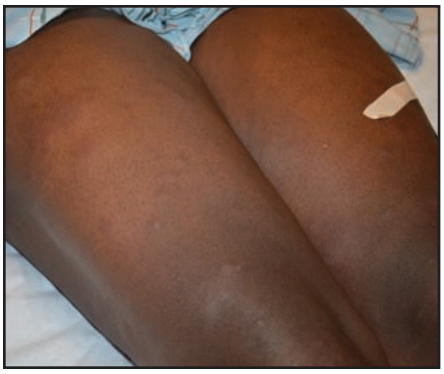
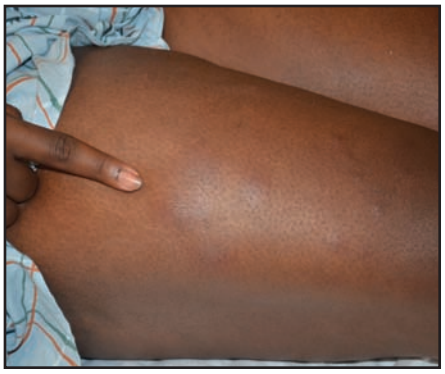
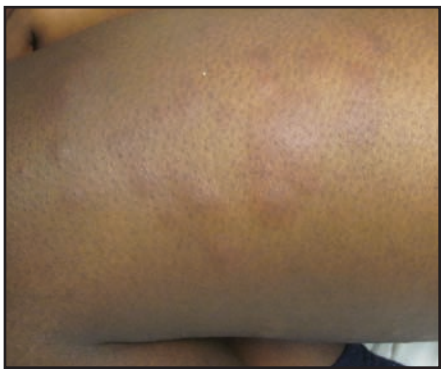
Microscopic Findings and Clinical Course

The biopsy revealed a neutrophilic infiltrate involving the dermis (Figure 2) that extended into the subcutaneous adipose tissue (Figure 3). Additionally, a medium-sized vasculitis was seen with leukocytoclasis and extravasation of red blood cells (Figure 4). Acid fast bacteria, gram, and dieterle (for treponema and mycobacterium) stains failed to reveal micro-organisms. After skin biopsy confirmation, the patient was diagnosed with subcutaneous Sweet's syndrome and subsequently started on prednisone 60mg by mouth daily and indomethacin 25mg by mouth three times per day. The patient's fever and lesion pain rapidly defervesced after the initiation of therapy. Clinical examination by Day 5 of hospitalization showed no evidence of nodules. An extensive workup for systemic hematological disease, infection, inflammation, and malignancy was sought without any results. At one month post-therapy, the patient is clear of clinical disease and back to his usual state of health.

Discussion

Sweet's syndrome, or acute febrile neutrophilic dermatitis, is characterized by the rapid onset of systemic symptoms, such as fever and fatigue with symmetrical, tender, indurated, and warm nodules and/or plaques. It is most commonly seen on the extremities or face and neck of middle aged individuals roughly 30 to 60 years old and seen much less often in children and adolescents.[1] Sweet's syndrome is defined by a dermal infiltrate of mature neutrophils and thought to be a reactive process (hypersensitivity reaction) to a systemic factor, such as hematological disease, infection, inflammatory disease, vaccination, drug exposure, and/or malignancy,[2] although about 40 percent of cases are idiopathic.[3]

Sweet's syndrome was first described by Dr. Robert Douglas Sweet in 1964, and, since then, there have been several hundred cases published. However, the subcutaneous variant characterized by an infiltrate that predominates in the fat lobules (neutrophilic panniculitis) is rarely seen.[1,2,4] Fewer than 10 cases are reported in the literature, thus a precise incidence of the subcutaneous variant is difficult to know given many reports do not provide a detailed description of the specific location of the infiltrate. A revised diagnostic criteria for Sweet's syndrome were first proposed by Su

Figures 1A–1C. Multiple, tender, and erythematous nodules on the lower extremities

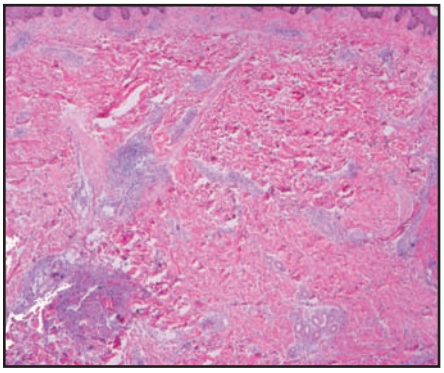


Figure 2. A neutrophilic infiltrate primarily involving the dermis is seen on scanning magnification.

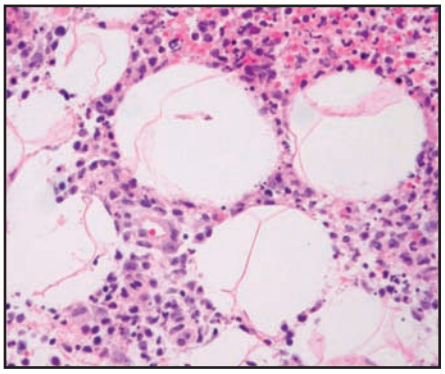


Figure 3. Upon closer inspection, the neutrophilic infiltrate appears to extend into the subcutaneous tissue.

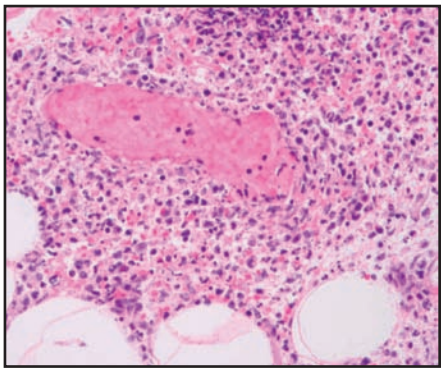


Figure 4. Leukocytoclasis, extravasation of red blood cells, and fibrinoid necrosis seen on deep inspection of the subcutis

and Liu in 1986[5] and then modified by von den Driesch in 1994,[6] requiring that two major and at least 2 of 4 minor criteria be fulfilled for diagnosis (Table 1).

As described previously, the histopathology of Sweet's syndrome is a diffuse infiltrate of mature neutrophils in the upper dermis along with dermal edema and a lack of vasculitis. However, the recent literature suggests that the presence of vasculitis (likely a secondary phenomenon) does not preclude the diagnosis (Figure 4).[7,8] In the subcutaneous variant, also called Sweet's panniculitis, the pathological changes are either localized within the adipose tissue or involve both the dermis and the subcutaneous fat in a nonspecific pattern infiltrating the lobules, septae, or both (Figure 3).[9] This variant is far less common than classical dermal infiltrate of Sweet's syndrome and has a stronger association with myelodysplastic syndromes and hematological neoplasms.[10] Associated diseases described in patients who have subcutaneous Sweet's syndrome include acute myelogenous leukemia, multiple myeloma, breast cancer, *Salmonella enteritidis* infection, and myelodysplastic syndromes similar to those of classic Sweet's syndrome. Thus, an aggressive search for underlying conditions should be undertaken.

Treatment for all neutrophilic dermatoses include oral corticosteroids (start at 1mg/kg/day and taper), which should lead to a quick resolution of lesions, although alternative treatments include topical and injectable corticosteroids and medications that inhibit neutrophil chemotaxis/function, such as indomethacin, colchicine, dapsone, and supersaturated solution of potassium iodide.[11,12] If an underlying cause is determined, it should be treated, as successful therapy may promote clinical resolution and limit recurrences.

TABLE 1. Diagnostic criteria for Sweet's syndrome variants

CRITERIA	CLASSIC/MALIGNANCY-INDUCED	DRUG-INDUCED	SUBCUTANEOUS
1	Acute onset of tender or painful erythematous plaques or nodules	Acute onset of tender or painful erythematous plaques or nodules	Acute onset of tender or painful erythematous plaques or nodules
2	Predominate neutrophilic infiltrate of dermis seen on histology	Predominate neutrophilic infiltrate of dermis seen on histology	Lobular infiltrate of neutrophils seen on histology, +/- infiltration of dermis
3	Accompanied by systemic symptoms, such as fever and malaise	Accompanied by systemic symptoms, such as fever and malaise	Accompanied by systemic symptoms, such as fever and malaise
4	Preceded by a vaccination or nonspecific respiratory or gastrointestinal infection or history of an inflammatory disease, malignancy, or current pregnancy	Temporal relationship between drug ingestion and clinical presentation or temporally related recurrence after oral challenge	Associated with myelodysplasia
5	Abnormal initial laboratory values of: ESR >20; CRP positive; neutrophils >70% on peripherial blood smear; WBC >8000 (3 of 4 of these values necessary)	Temporally related resolution of lesions after drug withdrawal or treatment with systemic corticosteriods	Highly responsive to systemic corticosteriods
6	Excellent clinical response to treatment with systemic corticosteriods or potassium iodide	N/A	Neutrophilic infiltrate does not predominate in septa
7	N/A	N/A	No associated vasculitis
8	N/A	N/A	Other causes of panniculitis are excluded
DIAGNOSIS			
	Both major criteria (1 and 2) and 2 of 4 minor criteria (3–6) met	All 5 criteria met	Most or all of positive (1–5) and negative (6–8) criteria met

ESR=erythrocyte sedimentation rate; CRP=C-reactive protein; WBC=white blood cell count
Adapted from: Von den Driesch P. Sweet's syndrome (acute febrile neutrophilic dermatosis). *J Am Acad Dermatol.* 1994;31:535–556; Sutra-Loubet C, Carlotti A, Guillemette J, Wallach D. Neutrophilic panniculitis. *J Am Acad Dermatol.* 2004;50:280–285; Walker DC, Cohen PR. Trimethoprim-sulfamethoxazole-associated acute febrile neutrophilic dermatosis: case report and review of drug-induced Sweet's syndrome. *J Am Acad Dermatol.* 1996;34:918–923.

There is no standard on how to monitor patients with idiopathic Sweet's syndrome, as it may be a harbinger of an underlying systemic condition; as such, there is no consensus on monitoring patients with idiopathic involvement after complete disease remission.

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